

### **REMARKS**

Claims 12, 15, 20, 23, and 41 have been amended. Claims 33, 35 and 42-43 are canceled. Claims 13-14, 16-19, 21-22, 24, 26-27 and 34 were previously presented. New claim 44 has been added. Upon entry of this amendment, claims 12-16, 18-24, 26-27, 34, 41 and 44 will be pending. No new matter has been added.

The claim amendments and cancellations made herein have been made solely to expedite prosecution of the instant application and should not be construed as acquiescing to any of the Examiner's rejections.

Applicants note with appreciation the Examiner's reconsideration and withdrawal of the previous rejections of claims 20-21, 23-24, 26-27, 34 and 36 under 35 U.S.C. §102(e) and claims 12-16, 18-24, 26-27 and 33-36 under 35 U.S.C. §103(a).

#### **Allowable Subject Matter**

Applicants note with appreciation the Examiner's indication that claims 12-16, 18-19, 34 and 41 would be in a condition for allowance once the objections raised in the outstanding Office Action are met.

#### **Claim Objections**

On pages 2-3 of the Office Action, claims 12, 20, and 43 and claims dependent therefrom are objected to because of the recitation of "identifying the amino acid residues....in order to generate a three-dimensional model..." in steps (b) of claims 12 and 20 and step (c) of claim 43, followed by a step of "employing said three-dimensional model from step (b)."

Claim 43 has been canceled, thus obviating this rejection. The objection as applied to claims 12 and 20 has been met by the amendment of these claims to delete the phrase "in order to generate" and recite an active step of "generating a three-dimensional model of the APP-binding site of BACE ...." as suggested by the Examiner.

On page 3 of the Office Action, claims 41-42 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Claim 41 has been amended to be in independent form, as suggested by the Examiner. Claim 42 has been canceled, thereby obviating this rejection.

On page 3 of the Office Action, claim 43 and claims dependent therefrom are objected to in the recitation of “generating a three-dimensional representation from the three-dimensional coordinates ...” in step (b) and “identifying the amino acid residues forming the APP-binding site ...” in step (c) because the 3-D representation formed in step (b) is not required to have the 3-D coordinates of the complex of step (a), and thus is not required to have the recited BACE amino acids. Claim 43 has been canceled, thus obviating this rejection.

In view of the foregoing, reconsideration and withdrawal of the objection of claims 12, 20, and 43 are respectfully requested.

Rejection of Claims 20-24, 26-27, and 42 under 35 U.S.C. §112, Second Paragraph

On page 4 of the Office Action, claims 20-24, 26-27, and 42 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

According to the Office:

Claim 20 (claims 21-24, 26-27, and 42 dependent therefrom) is confusing in that step (d) recites “synthesizing said candidate agent”, which is followed by step (e) reciting “contacting said candidate agent with the three-dimensional model...” The term “synthesizing” would typically be interpreted by a skilled artisan as meaning physically preparing the candidate agent by a chemical synthetic process. However, the three-dimensional model of step (e) of claim 20 is interpreted as being a computer-generated representation and it is unclear as to how one contacts a physical agent with a computer-generated “three-dimensional model”.

This rejection has been met by the amendment of claims 20 and 42 to recite “contacting said candidate agent with BACE to determine the ability of said candidate agent to interact or bind to BACE.” Reconsideration and withdrawal of the rejection of claims 20-24, 26, 27 and 42 is respectfully requested.

Claim Rejections - 35 U.S.C. §101

On pages 4-6 of the Office Action, the Office has maintained the rejection of claims 20-23 under 35 U.S.C. § 101 allegedly because the claimed invention is directed to non-statutory subject matter. According to the Office, the methods of claims 20-23 “encompass method steps that can occur solely within a computer and do not require a transformation of the data or a ‘useful, concrete and tangible result.’”

Without acquiescing to the Office's position and in the interest of expediting the current prosecution, this rejection has been met by amending independent claim 20 to clarify that steps (e) and (f) encompass the active physical steps of synthesizing said candidate agent and contacting said agent with BACE. Claims 21-23, which dependent from claim 20, incorporate the limitations from base claim 20. Therefore, the claims rejected by the Office incorporate one or more physical transformation steps to comply with the §101 standard as applied by the Office.

The Office's position is respectfully traversed insofar as it would be applied to newly added claim 44. Claim 44 is directed to a method for identifying a candidate agent that interacts with a beta-amyloid precursor protein (APP) binding site of Beta-site APP Cleaving Enzyme (BACE) that includes the steps of:

(a) utilizing the relative three-dimensional structural coordinates of a complex of a BACE peptide and an APP inhibitor according to Figures 1A-1EEE,  $\pm$  a root mean square deviation from the backbone atoms of the amino acid residues in the complex of not more than 1.5Å, to generate a three-dimensional representation of the complex, wherein the BACE peptide in the complex consists essentially of the amino acid sequence of residues 58-447 of SEQ ID NO:1, and the APP inhibitor in the complex consists essentially of the amino acid sequence SEVNStaVAEF (SEQ ID NO:3), wherein Sta is (S)-statine;

(b) identifying the amino acid residues forming the APP-binding site of the BACE peptide from the three-dimensional representation in step (a);

(c) generating a three-dimensional model of the APP-binding site of BACE, wherein the APP-binding site comprises the relative structural coordinates according to Figures 1A-1EEE of amino acid residues LYS70, SER71, GLY72, GLN73, GLY74, TYR75, LEU91, VAL92, ASP93, THR94, GLY95, SER96, SER97, ASN98, TYR129, VAL130, PRO131, TYR132, THR133, GLN134, GLY135, LYS136, TRP137, LYS168, PHE169, PHE170, ILE171, ASN172, SER174, TRP176, GLY178, ILE179, LEU180, GLY181, ALA183, TYR184, ALA185, GLU186, ILE187, ALA188, ARG189, PRO190, ASP191, ASP192, ARG256, TRP258, TYR259, TYR283, ASP284, LYS285, SER286, ILE287, VAL288, ASP289, SER290, GLY291, THR292, THR293, ASN294, LEU295, ARG296, GLY325, GLU326, ARG368, VAL370, LYS382, PHE383, ALA384, ILE385, SER386, GLN387, SER388, SER389, THR390, GLY391, THR392, VAL393, GLY395, ALA396, and ILE447,  $\pm$  a root mean square deviation from the backbone atoms of said amino acid residues of not more than 1.5Å;

(d) employing said three-dimensional model from step (c) to identify said candidate agent;

(e) obtaining said candidate agent; and

(f) contacting said candidate agent with the three-dimensional model of the APP-binding site of the BACE to determine the ability of said candidate agent to interact or bind to BACE, whereby the detection of the ability of said candidate agent to interact or bind to the BACE peptide identifies said candidate agent.

Applicants submit that newly added claim 44 is also directed to statutory subject matter in view of the recent decision by the Court of Appeals of the Federal Circuit (CAFC) in *In re Bernard L. Bilski and Rand A. Warsaw* (545 F.3d 943, Fed. Cir. 2008) where the standard for evaluating the patent eligibility of a claimed process under §101 was clarified. In the *Bilski* decision, the CAFC clearly stated that “a claimed process is surely patent-eligible under §101 if: (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing.” *Id.* at 954. In adopting the “machine-or-transformation” test, the CAFC rejected several previous articulations of §101 tests, including the *Freeman-Walter-Abele* test requiring application of an “algorithm” to physical elements or process steps; the “useful, concrete and tangible result” test associate with the *State Street* decision (*State St. Bank & Trust Co. v. Signature Fin. Group*, 149 F.3d 1368, 1373 (Fed. Cir. 1998), which was alluded to in the previous Office Action dated January 7, 2008); as well as the “technological arts test.” The CAFC in *Bilski* concluded that the transformation step in a process does not require a physical transformation to be directed to patent eligible subject matter. In fact, the CAFC citing the decision in *Abele*, 684 F.2d 902, 908-09 (CCPA 1982), stated that transformation of x-ray data into a two-dimensional visual depiction on a display was sufficient to meet the transformation test, and was therefore considered to be patent-eligible subject matter. In this regard, the CAFC in the *Bilski* decision stated that:

This data [referring to the X-ray attenuation data produced in a two dimensional field] clearly represented physical and tangible objects, namely the structures of bones, organs, and other body tissues. Thus, the transformation of that raw data into a particular visual depiction of a physical object on a display was sufficient to render that more narrowly-claimed process patent-eligible. *Bilski*, 545 F.3d at 963-963.

The steps recited in claim 44 are similar to the x-ray visual depiction which was found to comply with the requirements of §101 in the *Abele* case. In particular, claim 44 includes the

steps of “(a) utilizing the relative three-dimensional structural coordinates of a complex of a BACE peptide and an APP inhibitor according to Figures 1A-1EEE, within the deviation specified, to generate a three-dimensional representation of the complex, wherein the BACE peptide in the complex consists essentially of the amino acid sequence specified;” “(b) identifying the amino acid residues forming the APP-binding site of the BACE peptide from the three-dimensional representation in step (a);” and “(c) generating a three-dimensional model of the APP-binding site of BACE, wherein the APP-binding site comprises the relative structural coordinates according to Figures 1A-1EEE of amino acid residues specified, within the deviation specified.” In the instant case, the three-dimensional structural coordinates of the complex of a BACE peptide and an APP inhibitor are analogous to the structures of the bones, organs and other body tissues in the *Abele* case. *See id.* Claim 44 requires a visual representation of these structural coordinates in a visual depiction of the ATP-binding site of BACE in step (b) or the three-dimensional model in step (c) that is used in the identification/selection of the candidate agents. Thus, as articulated in the *Bilski* decision, claim 44 requires transformation of the coordinate raw data into a particular depiction of a physical object on a display. *See id.* Accordingly, Applicants respectfully submit that claim 44 meets at least the transformation test as articulated by the CAFC in the *Bilski* decision, and should be considered to be patent-eligible under §101.

#### Claim Rejections – 35 USC § 112, First Paragraph, Written Description

On pages 6-9 of the Office Action, the Office has maintained the written description rejection of claims 33, 35, and 43 under 35 U.S.C. § 112, first paragraph.

Claims 33, 35 and 43 have been canceled, thus obviating this rejection.

#### Claim Rejections – 35 USC § 112, First Paragraph, Enablement

On pages 9-12 of the Office Action, the Office has maintained the enablement rejection of claims 33, 35, and 43 under 35 U.S.C. 112, first paragraph.

Claims 33, 35 and 43 have been canceled, thus obviating this rejection.

**CONCLUSION**

In view of the foregoing amendments and remarks, reconsideration is respectfully requested. This application should now be in condition for allowance; a notice to this effect is respectfully requested. If the Examiner believes, after this amendment, that the application is not in condition for allowance, the Examiner is requested to call the Applicant's attorney at the telephone number listed below.

A Request for Continued Examination (RCE), petition for extension of time, and appropriate fees are being submitted concurrently herewith. If there is an additional fee occasioned by this response that is not covered by an accompanying Deposit Account authorization, please charge any deficiency to Deposit Account No. 50-2762, referencing Attorney Docket No. W2025-701110.

Respectfully submitted,  
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